UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,344	05/15/2006	Eng H. Lo	M0765.70047US01	6440

23628 7590 11/29/2007
WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

EXAMINER	
GUCKER, STEPHEN	
ART UNIT	PAPER NUMBER
1649	
MAIL DATE	DELIVERY MODE
11/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,344	LO ET AL.	
	Examiner	Art Unit	
	Stephen Gucker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,29-33,42 and 43* is/are pending in the application.

4a) Of the above claim(s) *29-33,42 and 43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/5/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 1-13, drawn to a method of treatment by administering an agent, classification dependent on the chemical nature of the agent.

Group II, claims 29-33, drawn to a method of identifying a candidate agent, classification dependent on the chemical nature of the agent.

Group III, claims 42-43, drawn to a method of making and identifying a tissue plasminogen activator (tPA) variant, classified in class 435, subclass 7.1+, for example.

2. The technical feature of Group I is a method of treatment by administering an agent that reduces binding between tPA and LRP. However, this was not a contribution over the prior art as Higazi discloses the same invention (see Example 3 and claims 9 and 10). Because the technical feature of Group I is not a contribution over the prior art, the Group I technical feature is not a special technical feature by definition and thus the inventions lack unity.

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim

remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1. 1741).

4. During a telephone conversation with MaryDilys. S. Anderson on 11/15/07, a provisional election was made with traverse to prosecute the invention of Group I, claims 1-13. Affirmation of this election must be made by applicant in replying to this Office action. Claims 29-33 and 42-43 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for agents that reduce tissue plasminogen activator (tPA) binding to the low-density lipoprotein-receptor-related protein (LRP) wherein the agent is an antibody or antigen-binding fragment, does not reasonably provide enablement for other types of agents or to other types of low-density lipoprotein-receptor-related protein receptors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The factors that are considered when determining whether a disclosure satisfies enablement

requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the claims. *Ex Parte Forman*, 230 USPQ 546 (Bd Pat. App. & Int. 1986); *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988). The specification provides no working examples of a method of treatment using any agent to reduce binding of tPA and LRP. However, it does provide direction and guidance prophetically that the method may be performed by using antibodies or antigen binding antibody fragments on page 22. These antibodies may be produced by using LRP as an antigen. No adequate direction or guidance is provided for producing other agents that reduce binding of tPA and LRP because the specification does not provide any examples of a specific polypeptide or other chemical agent to use as a starting point to enable the extremely broad genus of "agents" which may be any product that possesses the desired function of reducing binding. Since no specific species is given as a starting point, the quantity of experimentation necessary is undue since every possible agent regardless of chemical composition or structure may be encompassed by the extremely broad claims since the specification does not provide any specific species as a starting point in order to reduce the amount of experimentation necessary, and it is not predictable given the teachings of the disclosure what agents may or may not work as intended by the claim language. In addition, both the prior art and the specification identify the receptor that mediates the side effects of tPA therapy as the

low-density lipoprotein-receptor-related protein (LRP) (note that the word "receptor" does not follow the abbreviation "LRP" in the prior art), and not any of the other members of the low density lipoprotein (LDL) receptor family as discussed on instant page 9. Therefore, claims reciting "a" low-density lipoprotein-receptor-related protein (LRP) are of undue scope because it is entirely unpredictable what other receptors in this family may or not mediate the disclosed side effects without forcing undue experimentation to be performed. Furthermore, the broad scope of any and all possible side effects of tPA therapy are not adequately supported by the disclosure (such as allergic reactions, etc.), so the claims should have the limitations found in claim 3.

8. Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Both the prior art and the specification identify the receptor that mediates the side effects of tPA therapy as the low-density lipoprotein-receptor-related protein (LRP) (note that the word "receptor" does not follow the abbreviation "LRP" in the prior art), and not any of the other members of the low density lipoprotein (LDL) receptor family as discussed on instant page 9. Because the specification does not describe any other specific receptors which mediate the side effects of tPA treatment, applicants do not possess the invention. Furthermore, the instant specification does not adequately describe, other than antibodies, the

specific chemical nature of other agents that may be used in the instant invention. Sufficient description to show possession of a genus may be achieved by means of a recitation of a representative number of receptors, polypeptides, or other agents falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. See *Ex parte Kubin*, 83 USPQ2d 1410 and *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. See *University of Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895. In this case, the disclosure only describes a method of reducing binding between the LRP and tPA by the use of antibodies in sufficient detail to demonstrate possession of the invention. Therefore, a sufficient number of species falling within the broad genus cannot be established to show possession of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed receptors or agents used in the process claims and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or

simplicity of the method of manufacturing or testing the claimed process. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for making or testing it. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. (See page 1115.). For the reasons given above, it is concluded that the inventors did not have possession of the claimed invention at the time the application was filed.

9. Claims 1, 3-5, and 11-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 does not recite any specific process steps by which the method may be performed, rendering the claims vague and indefinite in regards to the metes and bounds of the claims. Also, claim 5 is not further limiting of the independent claim 1.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1-13 are rejected under 35 U.S.C. 102(e) as being anticipated by Higazi (US 2003/0211095 A1). Higazi discloses methods using anti-LRP antibodies to reduce binding of tPA to LRP for the purpose of reducing the side effect of hemorrhaging in humans (abstract, Figure 3, paragraphs [0005], [0008], [0011], [0014], [0020], [0023], [0032-0033], [0044], [0048-0049], Example 3, and claims 9-10).

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is 571-272-0883. The examiner can normally be reached on Mondays through Fridays from 0930 to 1800.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen Gucker

November 26, 2007

JEFFREY STUCKER
SUPERVISORY PATENT EXAMINER